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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,072	GIRARD ET AL.	
	Examiner	Art Unit	
	Lei Yao, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-91* is/are pending in the application.

4a) Of the above claim(s) *1-14 and 29-91* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/14/05, etc*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II (claims 15-28) with species CCL5 in the reply filed on 5/15/06 is acknowledged. The traversal is on the ground(s) that examination of group II and group I (claims 1-14) together would not impose s serious burden.

Applicants argue that although group I and II are patentable distinct, these two groups can be examined together without serious burden because these are both groups are directed to similar, scientifically overlapping subject matter. **These have been considered, but not found persuasive.** As MPEP states "*Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects*" (MPEP § 806.04, MPEP § 808.01). The group I and II are two distinct inventions, which are drawn to the methods having different method steps, mode of operation, and effects. Searching two methods are not co-extensive in non-patent literature and US patent database, which would impose a serious search burden. For this reason, the restriction requirement is deemed to be proper and is adhered to. The requirement is therefore made **FINAL**.

After review and reconsideration of the elected species in light of the prior art, the species SLC/ CCL21 is joined to the species of CCL21 for examination at this time.

Claims 1-91 are pending. Claims 1-14 and 29-91 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions or non-elected species. Claims 15- 28 (group II) with species CCL5 and SLC/CCL21 will be examined on the merits.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 1/15/04. 1/24/04, 3/14/05, 12/21/04, 1/26/04 are/is considered by the examiner and initialed copies of the PTO-1449 are enclosed.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Applicant's claims to an earlier effective filing date through US provisional application, 60/432699 ('699), filed on Dec 10, 2002, 60/341997 ('997), filed on Dec 18, 2001, and is a CIP of US application 10/317832 ('832) filed Dec 10, 2002 are Acknowledged. However, upon review of specification of the provisional applications as well as application '832, it is noted that none of the applications provides adequate support for elected claimed method of inhibiting the activity of a chemokine comprising contacting a chemokine with a THAP-1 and THAP-1 fragment with a chemokine binding domain, wherein the chemokine is CCL5 (elected species). Therefore, for the purposes of examining this application, the examiner has established the effective priority dated of June 19, 2003, the filing dated of the instant application. If applicants disagree with the rejection set forth in this office action base on this priority date, applicant is invited to submit evidence pointing to the serial number and pages to support the claimed priority date.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims are indefinite because the term "an effective amount of agent comprising a polypeptide" in claim 15 is not clear.

MPEP2173.05 state:

> *The common phrase" an effective amount" may or may not be indefinite. The proper test is whether or not one skilled in the art could determine specific values for the amount based on the disclosure.*

> *The phrase "an effective amount" has been held to be indefinite when the claim fails to state the function which is to be achieved and more than one effect can be implied from the specification or the relevant art. In re Fredericksen 213 F.2d 547, 102 USPQ 35 (CCPA 1954).*

The specification on paragraphs 947-948 in section of "reducing a chemokine medicated effect"" teaches "the THAP-type chemokine binding agents are administered to a subject in effective amounts so as to reduce the symptoms associated with the condition". However it does not teach what has been achieved in the treatment or whether the amount of the agent comprising polypeptide used in the treatment is therapeutically effective amount". Therefore, the metes and bounds of "an effective amount" in claim 15 cannot be determined because those skilled in the art would not be able to determine the effective amount of the agent comprising polypeptide used for claimed method. Claim 15 also renders the claims 16- 21 and 23-28 indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Drawn to written description- agent comprising THAP-1 variants:

Claims 15-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the instant case, the claims are drawn to a method of inhibiting the activity of a chemokine comprising contacting the chemokine with an agent comprising polypeptides THAP-1, polypeptide having at least 30% amino acid identity to THAP-1, a polypeptide having at least 30% amino acid identity to THAP-1, and a polypeptide having at least 30% of amino acid identity to chemokine-binding domain comprising amino acid 143-213 of SEQ ID NO: 3, wherein the activity of said chemokine is inhibited. Thus, the claims are an inclusive of a genus of chemokine binding or inhibiting agents or peptides

comprising THAP-1 polypeptide variants and homologs, or any chemokine binding agent having a 30% amino acid identity to chemokine binding domain of THAP-1 without defining the structure of the agent or the peptides. However, the written description (specification, page 230-232, example 14-17) only reasonably set forth a polypeptide at amino acid residues 143-213 of THAP1, SEQ ID NO: 3, that is associated with a chemokine SLC/CCL21 binding activity and THAP1 protein that is associated with binding CCL5 and SLC/CCL21 chemokines to inhibit chemokine activity (example 34-37, page 252-259). The written description does not provided any teaching that any other agent comprising any other peptide of fragment variants of THAP-1 that at are 30% identity to the binding domain of THAP1 that bind to any chemokine including claimed chemokines, CCL5 and SLC/CCL21, and inhibit the activity of chemokine.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics. i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613.

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a

representative number of polypeptide variants of THAP1 having a 30% identity to chemokine binding domain of THAP1 that encompass the genus that reveal the roles of these polypeptides in the binding to chemokines comprising CCL5 and SLC/CCL21 nor does it provide a description of structural features that are common to the chemokine binding domain of THAP1 comprising amino acids 143-213 of SEQ ID NO: 3) that bind to a chemokine comprising CCL5 or SLC/CCL21. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of *the* species of the polypeptide, THAP1 protein or 143-213 of SEQ IDNO: 3 is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) and functional attribute(s) of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the method of inhibiting the activity of CCL5 or SLCCCL21 by contacting the polypeptides consisting of amino acid sequence 143-213 of SEQ ID NO: 3 binding to SLC/CCL21 and THAP1 protein binding to CCL5 and SLC/CCL21, but not the full breadth of the claims, meets the written

description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Enablement

Claims 15-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting chemokine activity by contacting a polypeptide at amino acid residues 143-213 of THAP1 (SEQ ID NO: 3) that binds to SLC/CCL21_binding activity and THAP1 protein (SEQ ID N O:3) that binds to CCL5 and SLC/CCL21, does not reasonably provide enablement for **A)** the method by contacting any other agent comprising polypeptide variants of THAP1 having 30% amino acid identity that are associated with binding chemokines comprising CCL5 and SLC/CCL21 and **B)** the method by contacting the chemokine binding domain comprising143-213 of THAP of SEQ IDN O:3 to any chemokine other than CCL5 or CCL21. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factor considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re wands,* 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are broadly drawn to a method of inhibiting the activity of a chemokine comprising contacting a chemokine with an agent comprising polypeptides having at least 30% amino acid identity to chemokine-binding domain of amino acid residues 143-213 of SEQ ID NO: 3, wherein the activity of said chemokine is inhibited. However, the specification, on page 230 (example 15-17)only teach a polypeptide at amino acid residues 143-213 of THAP1, SEQ ID NO: 3, that is associated with a chemokine SLC/CCL21 binding and on p252-259 (example 32-37) teach that THAP1 protein is associated with

SLC/CCL21 and CCL5 binding and inhibition of the chemokine activity . The specification does not provided any teaching or working example to show that any other agents comprising any polypeptide variant of THAP-1 having a 30% identity to the chemokine binding domain of 143-213 of SEQ ID NO: 3 that is associated with chemokine binding and inhibiting the activity of the chemokine. The specification also fails to provide any teaching or working example to show the chemokine binding domain of amino acid residues 143-213 of THAP1, SEQ ID NO: 3, or THAP1 protein self having a binding ability to all of the chemokines.

It is also know in the art that even a single modification or substitution in a protein sequence can alter the protein function. Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (**Burgess et al,** Journal of Cell biology, Vol 111, p2129-2138, 1990). Removal of the amino terminal histidine of glucagons substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase **(Lin et al** Biochemistry USA, vol 14, p1559-1563, 1975). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein.

Since the specification does not provide claimed method of inhibiting the activity of a chemokine by contacting a chemokine with an agent comprising a polypeptide having 30% identity to the chemokine binding domain comprising amino acid 143-213 of THAP1 (SEQ ID N O:3) or by contacting chemokine binding domain of THAP1 comprising amino acid 143-213 of THAP1 or THAP1 protein to any chemokine other than CCL5 or SLC/CCL21, since the specification does not provide any guidance for how to use the claimed method, one skilled in the art would not know how to use the claimed agent comprising polypeptide variants of chemokine binding domain of THAP1 for inhibiting the chemokine activity on the basis of teachings in the prior art or instant specification.

In view of the lack of guidance, lack of examples, and lack of predictability associated with inhibiting chemokine activity by binding to a chemokine with a agent comprising THAP1 chemokine

binding domain variants, one skilled in the art would be forced into under experimentation in order to practice the broadly claimed invention. If Applicants has any objective evidence contrary to the rejection, Applicant is invited to submit it to the Office for reconsideration.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

1. Kawai et al., (J Immun. Vol 163, 3269-3278, 1999) disclose a method of inhibition of chemokine activity by contacting an antibody to RANTES, another name of CCL5. Kawai et al., do not teach or suggest inhibiting chemokine activity comprising activity of CCL5 by contacting THAP1 protein or its fragments or variants.

2. Tang et al., (WO200157190, published date, 8/9/2001) disclose a protein comprising an amino acids 143-213 of SEQ ID NO: 3. Tang et al., do not teach or suggest that the protein has a chemokine binding or inhibiting activity.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-4.30pm Monday to Friday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner
Art Unit 1642

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

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